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09/828,574	04/06/2001	Salvatore Albani	UCSD1310-1	6601

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EXAMINER
NAVARRO, ALBERT MARK

ART UNIT	PAPER NUMBER
1645	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/828,574	Applicant(s) Albani et al
	Examiner Mark Navarro	Art Unit 1645

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on _____.

2a) This action is **FINAL**. 2b) X This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-59* is/are pending in the application.

4a) Of the above, claim(s) *25-32 and 43-59* is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) X Claim(s) *1-24 and 33-42* is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) X Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1	X Notice of References Cited PTO-892	4	Interview Summary PTO-413 Paper No s.
2	Notice of Draftsperson s Patent Drawing Review PTO-948	5	Notice of Informal Patent Application PTO-152
3	Information Disclosure Statement s PTO-1449 Paper No s.	6	Other

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-24 and 33-42 in Paper No. 11, received July 29, 2002 is acknowledged. The traversal is on the ground(s) that each of the recited sequences are HLA pan DR-binding peptides. Applicant's further assert that MPEP 806.05(h) provides that distinction between a product and process of using can be shown (A) if the process of using as claimed can be practiced with another materially different product, or (B) if the product as claimed can be used in a materially different process. Applicant's further assert that the distinction between the methods of Groups IV and V may be found in a difference in the selection of a patient with different symptoms, and assert that the condition of a particular patient is not relevant to the claimed methods.

First, the requirement for restriction to a particular sequence is withdrawn in view that each of the recited sequences are HLA pan DR-binding peptides.

Applicant's further assert that the restriction between Groups I and IV & V is subject to the requirements set forth in MPEP 806.05(h). This is readily agreed to. As set forth in MPEP 806.05(h) restriction is proper if (A) the process of using as claimed can be practiced with another materially different product, or (B) if the product as claimed can be used in a materially different process. In the instantly filed application the claimed product (i.e., peptides) can be used to

modulate an immune response in vivo as claimed, or alternatively may be incorporated into an in vitro assay to screen for the presence of antibodies. Consequently the requirements of MPEP 806.05(h) have been fully complied adhered to. Finally, Applicant's assert that the distinction between the methods of Groups IV and V may be found in a difference in the selection of a patient with different symptoms, and assert that the condition of a particular patient is not relevant to the claimed methods. However, Applicant's are again reminded that according to MPEP 806.05(h) the elected group (peptides) can be used in a materially different process as shown above. Consequently, restriction between Groups I and IV & V is appropriate. It is noted that in light of Applicant's selection of the peptides of Group I rather than a method of treatment, election of a particular condition for treatment is not necessary.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. Claims 1-24 and 33-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is vague and indefinite in the recitation of a chain of amino acids "substantially pure peptide." One of skill in the art cannot determine the metes and bounds of such a limitation.

For instance, does the term substantially pure refer to 99.9% or 99% or 90% or 50% ... purity? Furthermore at what level of contaminants would the peptide no longer be substantially pure? Without a clear definition as to the metes and bounds of the phrase "substantially pure" one of skill in the art would be unable to determine the metes and bounds of the claimed invention.

As a suggestion amendment of the claims to recite "isolated" will be sufficient to overcome this rejection.

3. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is vague and indefinite in the recitation of a chain of amino acids "similar size, charge and/or polarity." One of skill in the art cannot determine the metes and bounds of such a limitation. For instance, does the term similar size refer to (e.g., same weight, same ring structure, approximate weight)? Furthermore at what level are molecules no longer of similar size or polarity (99%, 90%, 50% etc. identical)? Without a clear definition as to the metes and bounds of the phrase "similar size, charge and/or polarity" one of skill in the art would be unable to determine the metes and bounds of the claimed invention.

4. Claims 3-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite in the recitation of "conserved" One of skill in the art cannot determine the metes and bounds of such a limitation. For instance, does the term conserved require 99% identity or 90% identity, etc.? Furthermore at what level are molecules no longer conserved (90%, 70%, 50% etc. identical)? Without a clear definition as to the metes and bounds of the phrase "conserved" one of skill in the art would be unable to determine the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-19, 21, 24, and 33-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Thompson *et al.*

The claims are drawn to substantially pure HLA pan DR-binding peptides comprising a fragment of a stress protein that binds to one or more MHC class II molecules, wherein the peptide is selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9 and 10.

Thompson *et al* (WO 96/10039) disclose of polypeptide fragments for the use in prevention, diagnosis and treatment of auto-immune disease such as rheumatoid arthritis and methods of preparing the fragments. Thompson *et al* further disclose of the production of a fragment identical to SEQ ID NO: 4 of the instant invention. (See Figure 1 and claims).

In view that Thompson *et al* disclose of a peptide which is 100% identical to the peptide as claimed, the disclosure of Thompson *et al* is deemed to anticipate the claimed invention. It is noted that Thompson *et al* do not characterize the peptide as binding to one or more MCH class II molecules, however in view that the peptide is identical to the peptide as claimed, it is deemed to be an inherent characteristic of the claimed peptide.

6. Claims 1-17, 21, 24, and 33-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderton *et al*.

The claims are drawn to substantially pure HLA pan DR-binding peptides comprising a fragment of a stress protein that binds to one or more MHC class II molecules, wherein the peptide is selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9 and 10.

Anderton *et al* (WO 95/25744) disclose of peptide fragments which are useful for protection against or treatment of an inflammatory disease, including autoimmune diseases, such as diabetes, arthritic diseases, atherosclerosis, multiple sclerosis, myasthenia gravis, or inflammatory responses due to tumor or transplant rejection. Anderton *et al* further disclose of the production of a fragment identical to SEQ ID NO: 2 of the instant invention. (See Figure 13 and claims).

In view that Anderton *et al* disclose of a peptide which is 100% identical to the peptide as claimed, the disclosure of Anderton *et al* is deemed to anticipate the claimed invention. It is noted that Anderton *et al* do not characterize the peptide as binding to one or more MCH class II molecules, however in view that the peptide is identical to the peptide as claimed, it is deemed to be an inherent characteristic of the claimed peptide.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-24 and 33-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderton in view of Srivastava and Russel-Jones *et al* and Guichard *et al*.

The claims are drawn to substantially pure HLA pan DR-binding peptides comprising a fragment of a stress protein that binds to one or more MHC class II molecules, wherein the peptide is selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9 and 10; wherein the peptide has one or more D-amino acids, covalently liked to an adjuvant, and further comprises an interferon.

The teachings of Anderton *et al* are set forth above.

Anderton *et al* do not teach of the peptide having one or more D-amino acids, covalently liked to an adjuvant, and further comprises an interferon.

Srivastava (U.S. Patent Number 6,455,503) teach of stress protein-peptide complexes containing a therapeutically effective amount of a cytokine including IL-1, IL2 etc. Srivastava further sets forth that the cytotoxic T cell response may be enhanced by the presence of the cytokine. (See column 7 and claims).

Russel-Jones *et al* (U.S. Patent Number 5,928,644) teach of covalent attachment of BSA to a peptide antigen results is a significant enhancement of the immune response. (See columns 2-3).

Guichard *et al* (Proc. Natl. Acad. Sci. USA, Vol. 91, October 1994, pp 9765-9769) teach that the used of D amino acids to replace natural L-peptides results in peptides with a higher metabolic stability, since most natural proteases cannot cleave D-amino acid residues.

Given that 1) Anderton *et al* have taught of fragments of stress proteins which are identical to the instantly claimed fragments, (i.e., SEQ ID NO: 2), and that 2) Srivastava teaches of the desirability to incorporate cytokines with stress proteins, and that 3) Russel-Jones teaches that covalent attachment of BSA to a peptide results in significant enhancement of the immune response, and that 4) Guichard *et al* has taught that incorporation of D-amino acids into a peptide results in peptides with a higher metabolic stability, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have incorporated the cytokine with the stress protein as taught by Srivastava, or to the fused the antigen to BSA as taught by Russel-Jones *et al*, or to have incorporated a D-amino acid in the peptide antigen as taught by Guichard

et al. One would have been motivated to incorporate these changes in view of the advantageous properties displayed by the combination (i.e., increase CTL response, increased immune response, and increased stability), as set forth by Srivastava and Russel-Jones *et al* and Guichard *et al*.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

October 14, 2002